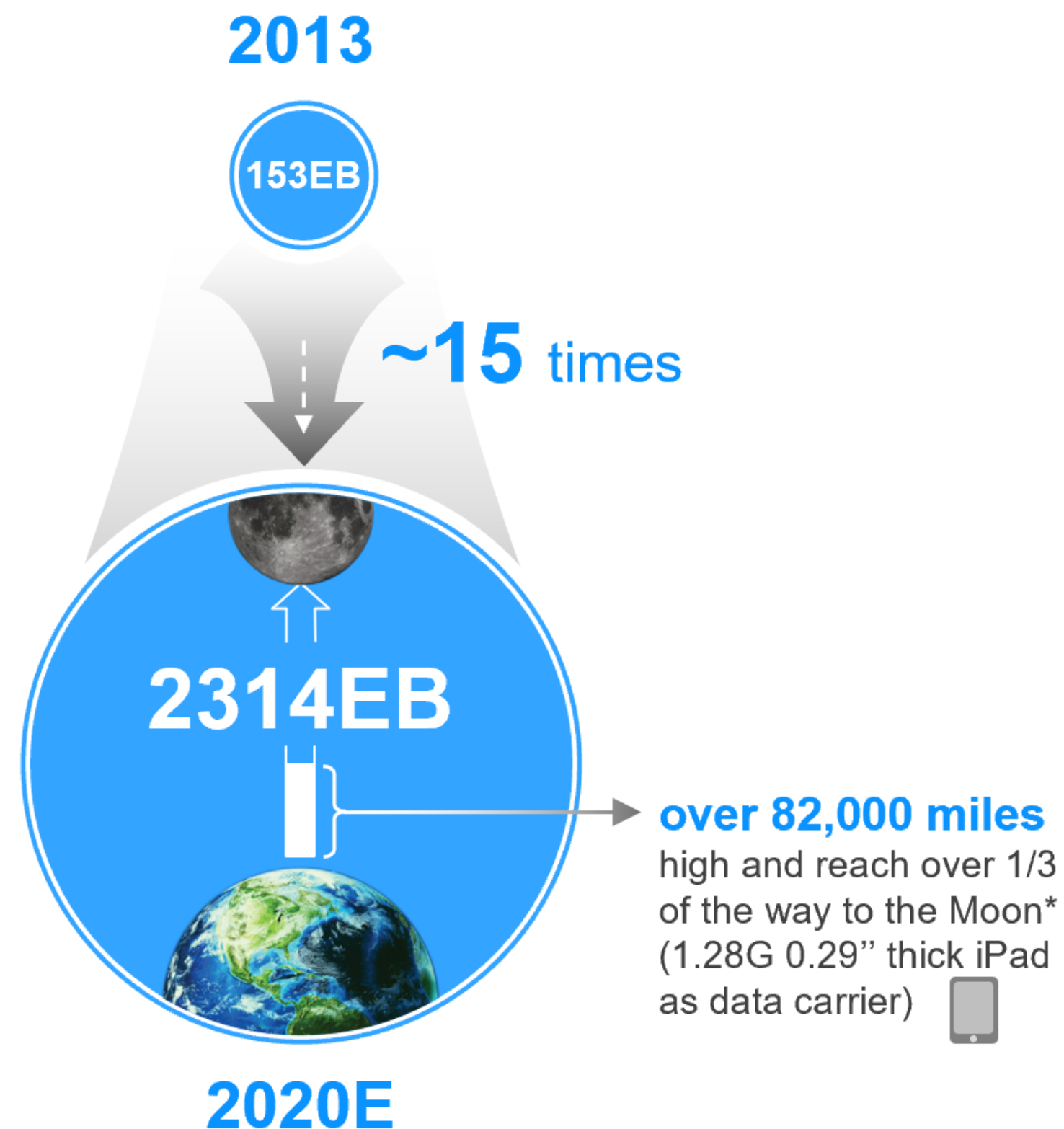




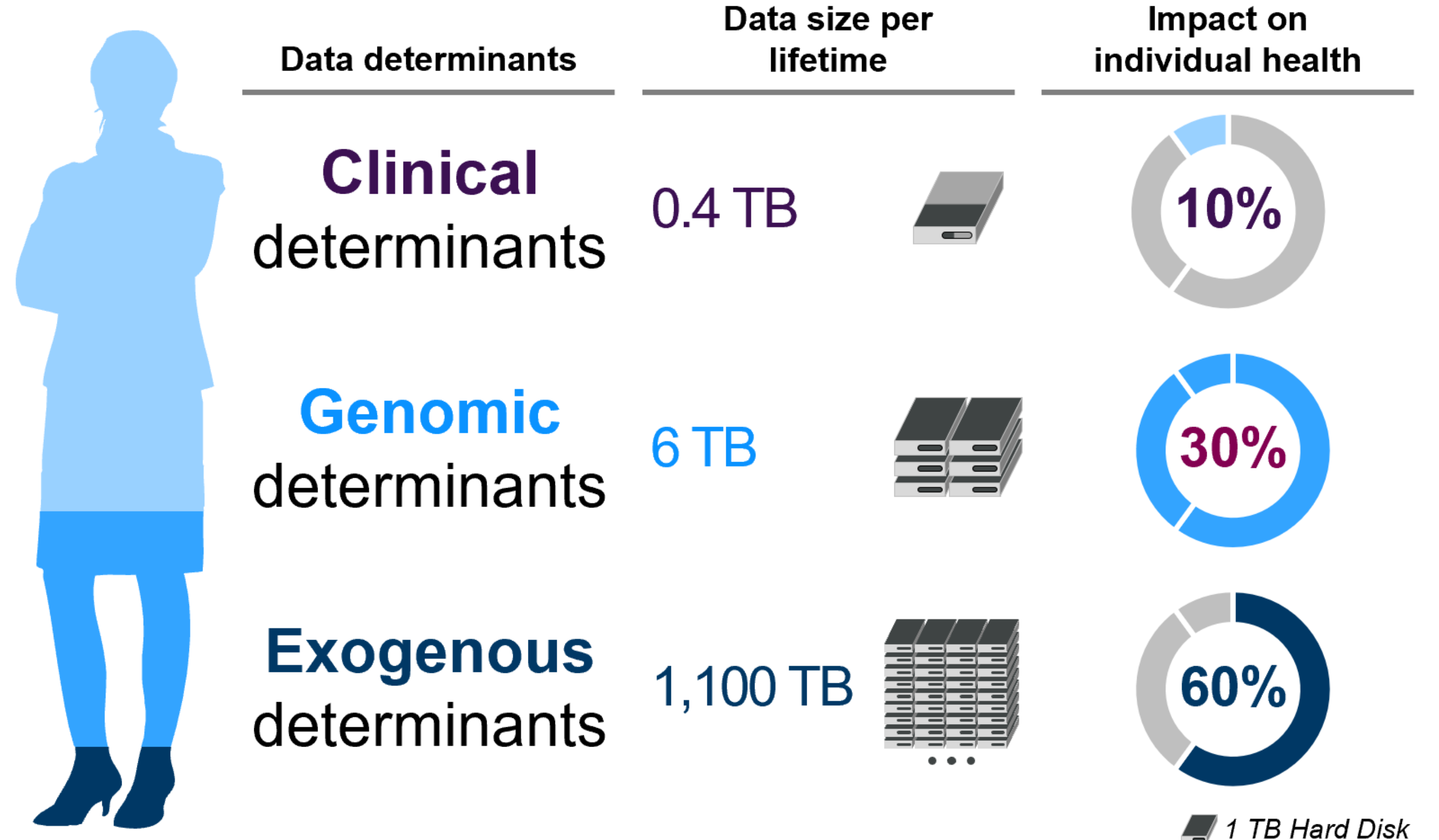
Big-Bang Of Real World Data (RWD) & Revolutionar y Market Insights Mining

RWD is booming globally, providing unprecedented opportunities for pharmacos to mine insights and develop new strategies

Global healthcare data size



Various source of health data



Source: The Digital Universe Driving Data Growth in Healthcare, IDC White Paper, 2014.

"The Relative Contribution of Multiple Determinants to Health Outcomes", Lauren McGover et al., Health Affairs, 33, no.2 (2018)

The pharm was looking for a holistic launch readiness partner with 3 unique challenges for a rare hematological disease

Key Issues in Launch Readiness Preparation

| | Patient Potential | Competitor | Access & Pricing | R&D |
|----------------|--|---|---|--|
| General Issues | <ul style="list-style-type: none"> • Patient subtype • Geographic distribution • Hospital concentration | <ul style="list-style-type: none"> • Competitive landscape • KOL mapping • Share erosion | <ul style="list-style-type: none"> • Reimb't impact • Price range • Innovative payment program | <ul style="list-style-type: none"> • Portfolio strategy • RCT feasibility • Registry roadmap • Subject recruitment |
| Unique Issue | <div>1</div> <ul style="list-style-type: none"> • % of patient with rare mutation • % of R/R¹ patient | <div>2</div> <ul style="list-style-type: none"> • Treatment choices for double genes mutated patient | <ul style="list-style-type: none"> • N/A | <div>3</div> <ul style="list-style-type: none"> • Opportunity of fast approval • Phase III acceleration |

Elaboration

Gene Mutation & R/R Rate

- 1
- How many China patients carry the rare mutation?
 - Cross sectionally, how many patients are R/R in China?

Mutation Diversity

- 2
- What's the distribution of patients with different mutation sites?
 - How many patients have multiple mutations at the same time?

Leapfrog Registry

- 3
- How to generate solid evidence to ensure fast approval application?
 - How to accelerate enrollment of patients with rare mutation?

Note: R/R = relapsed or refractory
 SOURCE: HLT experience



Take XXX as example, HLT platform has comprehensive and structure fields in medical record

| | | | |
|---|---------------------|--|------|
| 病理名称 | 病理 |  Pathologic diagnosis report | |
| 报告时间 | 2015-07-31 09:21:09 | | |
| 报告医师 | *** | | 审核医师 |
| 取材部位 | 骨髓 | | |
| | | | |
| 肉眼所见 | | | |
| 骨髓:骨髓样本3ml,无凝血,无溶血; | | | |
| | | | |
| 病理所见 | | | |
| 检测该样本中血液系统肿瘤密切相关的15个基因的全部外显子,结果如下: ; | | | |
| | | | |
| 病理诊断 | | | |
| 常规报告:送检标本中检测到 X 基因突变: ① X 基因编码序列发现 site 突变,此突变位点是 ABC 中的一个热点突变。② X 基因突变的, ABC 预后不良。送检标本中未检测出15个基因中的其它突变位点,此结果请结合临床及其他检查项目综合判断。; | | | |

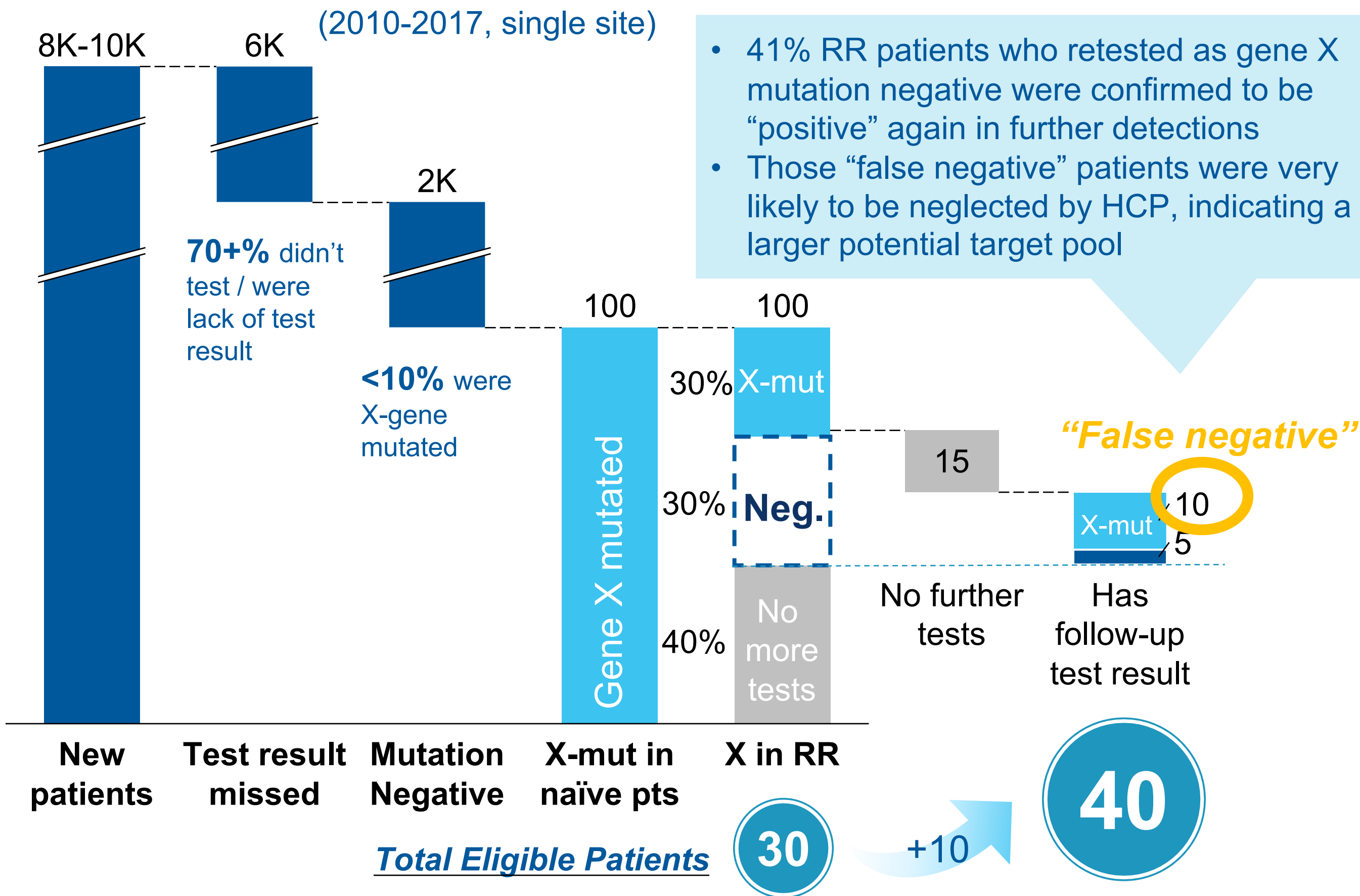
Discharge record

患者入院后体温正常，未诉特殊不适。查体：生命体征平稳。无贫血貌，周身皮肤无皮疹、黄染、出血点，浅表淋巴结无肿大。咽部无充血，扁桃体无肿大。胸骨无压痛，双肺听诊呼吸音粗，双下肺可闻及湿罗。心腹查体无异常。双下肢无水肿。检查结果：凝血八项（住院）：D-二聚体(定量) 0.74mg/LFEU1。血细胞分析（住
11.
7.8
+
支
气
管
解，
滨25mg×5d（2017.3.25-3.29、2017.5.16-5.20），后2017.8月予阿克拉霉素20mg/d×4d，阿糖胞苷100mg/d×6天，2017.9月再予米托蒽醌10mgD1、3+阿糖胞苷100mg×7d+环磷酰胺400mg/dD2、5化疗巩固后未再检查。目前疾病出现复发，考虑患者目前年龄较大，化疗可能耐受差，目前肾功能正常，无化疗

1

The “mutation ghost” was eventually proved to be “false-negative” due to specific treatment and forecast model assumption was also verified

Deep dive into false negative mutation patients



Implication

- Physician will still pursue complete remission among RR patients by adopting large chemo dosage, leading the mutation cell concentration level is too low to be detected
- Based on the “false-negative” insight to revise the forecast model, enlarging the eligible patient size in the market
- Develop market shaping strategy and message accordingly, to improve the awareness of “false-negative” mutation result

SOURCE: HLT experience

2

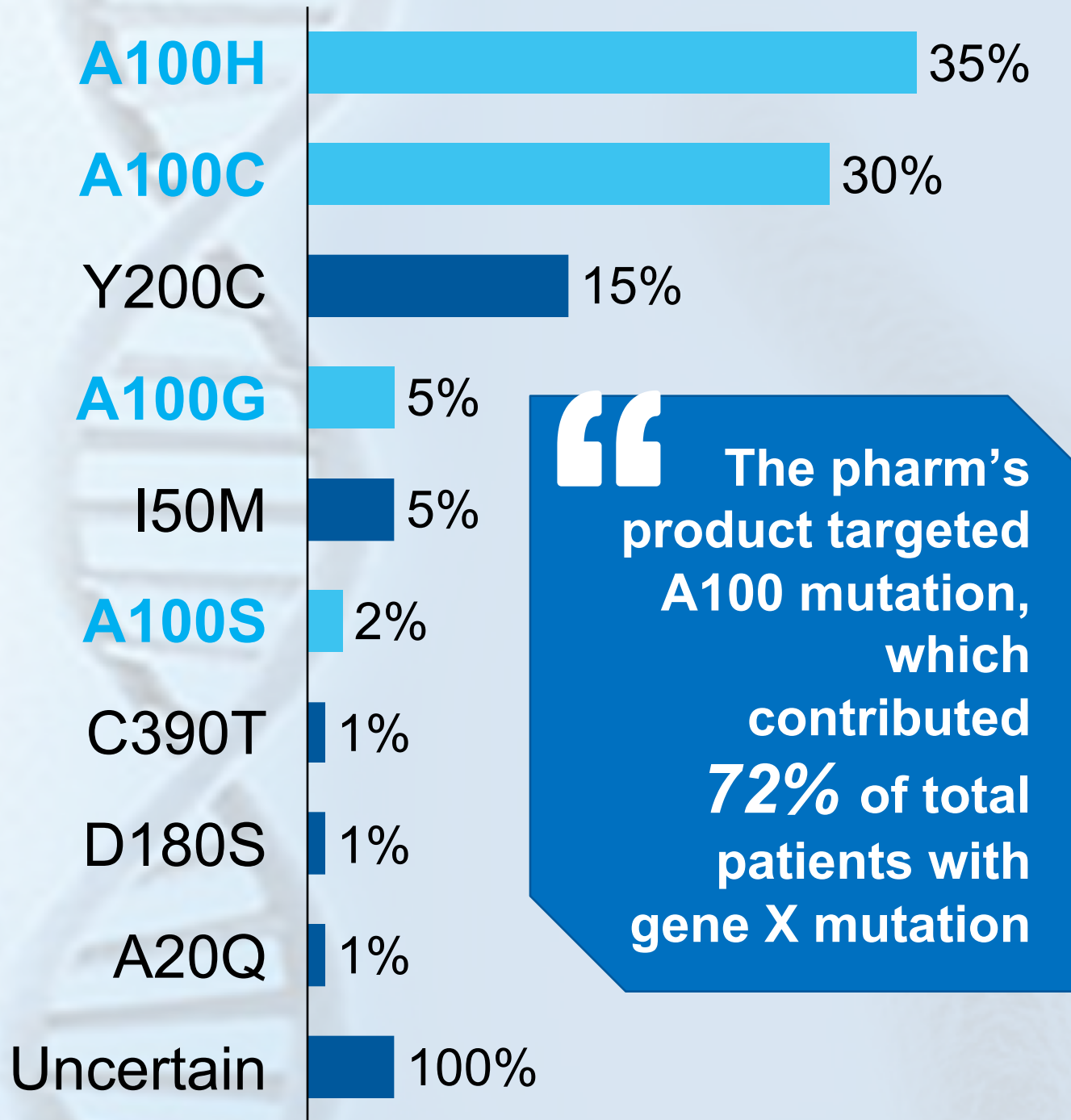
NGS demonstrated overlap rate between gene / site mutations, providing valuable information for competitor landscape & portfolio strategy

Implications

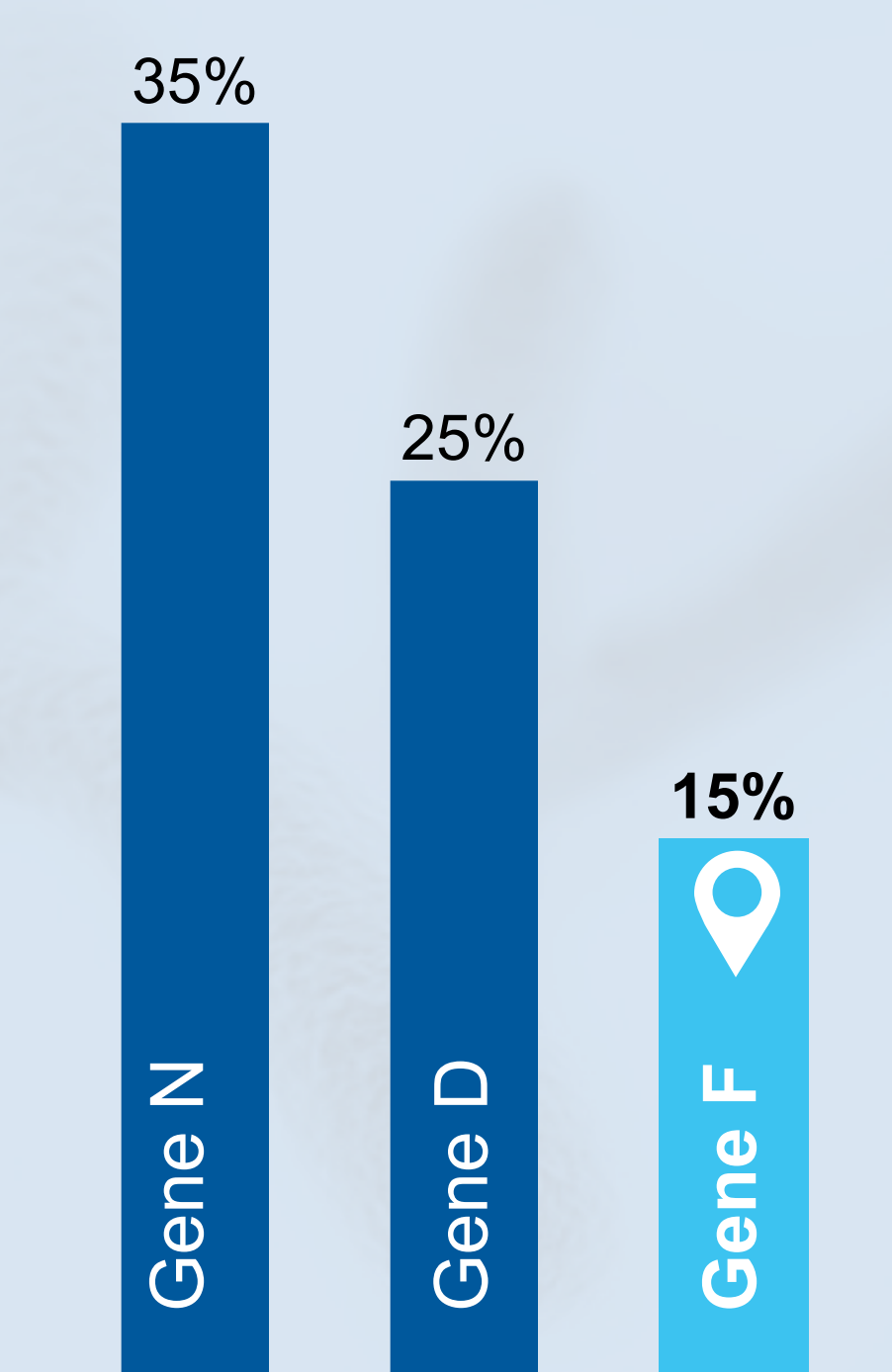
NGS and other lab test result description

.....为XX骨髓象，染色体45，X，t (x; xx)(qx; qx) [x]；组化示xx细胞比例增高；骨髓活检示ABC病。流式异常细胞占23.2%，表达XX分子，弱表达XX分子，不表达XX分子，符合XXX表型。XXX定量123.64%，F及D gene均阴性，肿瘤基因筛查K gene外显子17.....均阳性。融合基因-XXX 1/ETO(定量)123.6%。ABC诊断明确.....

% of patients by mutation sites of gene X



Overlap between gene X and other genes

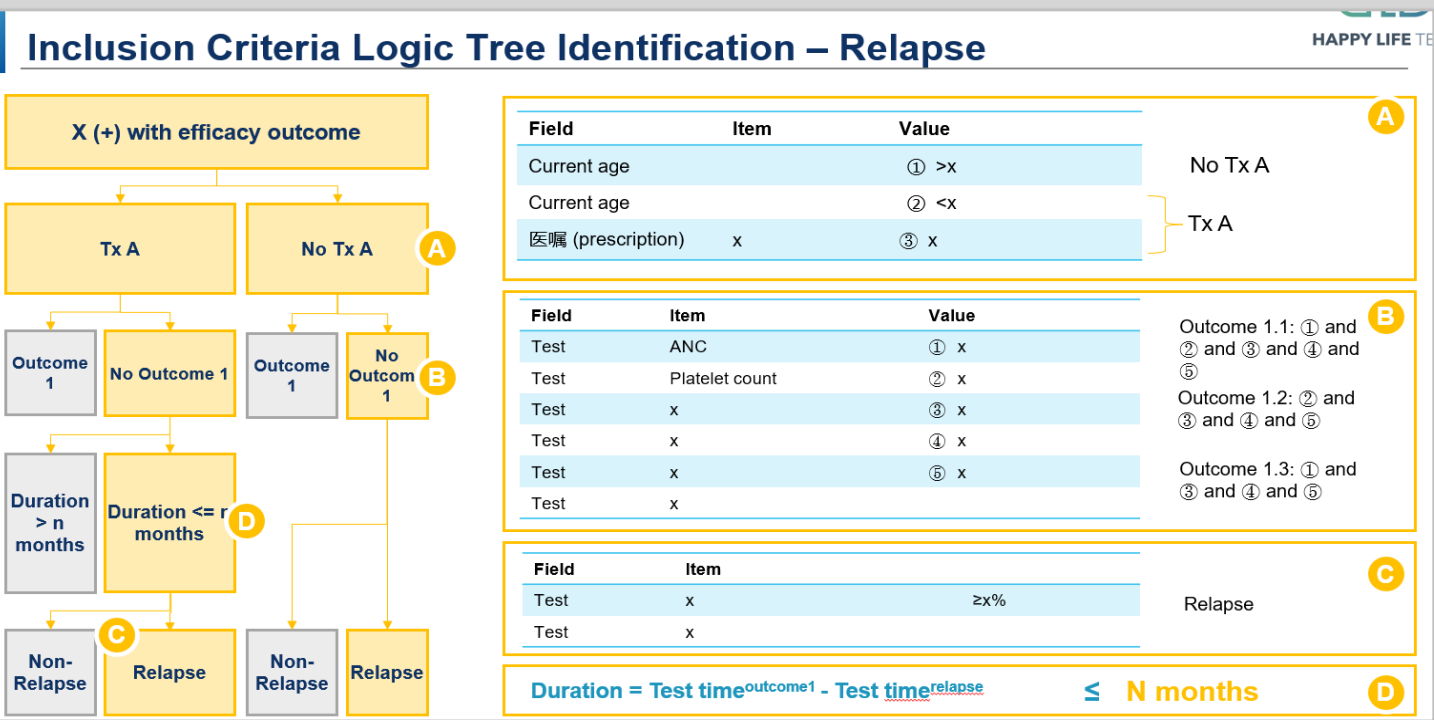


- ◆ RWD provided the solidest reference
 - Interview results varied greatly – “best guest” but not “evidence”
- ◆ Implication of portfolio strategy
 - Coexistence of gene X & F mutation was **15%**, without difference across mutation sites
 - Gene F inhibitor was more like a companion than competitor of gene X inhibitor. License-in of gene F inhibitor can be considered as well.

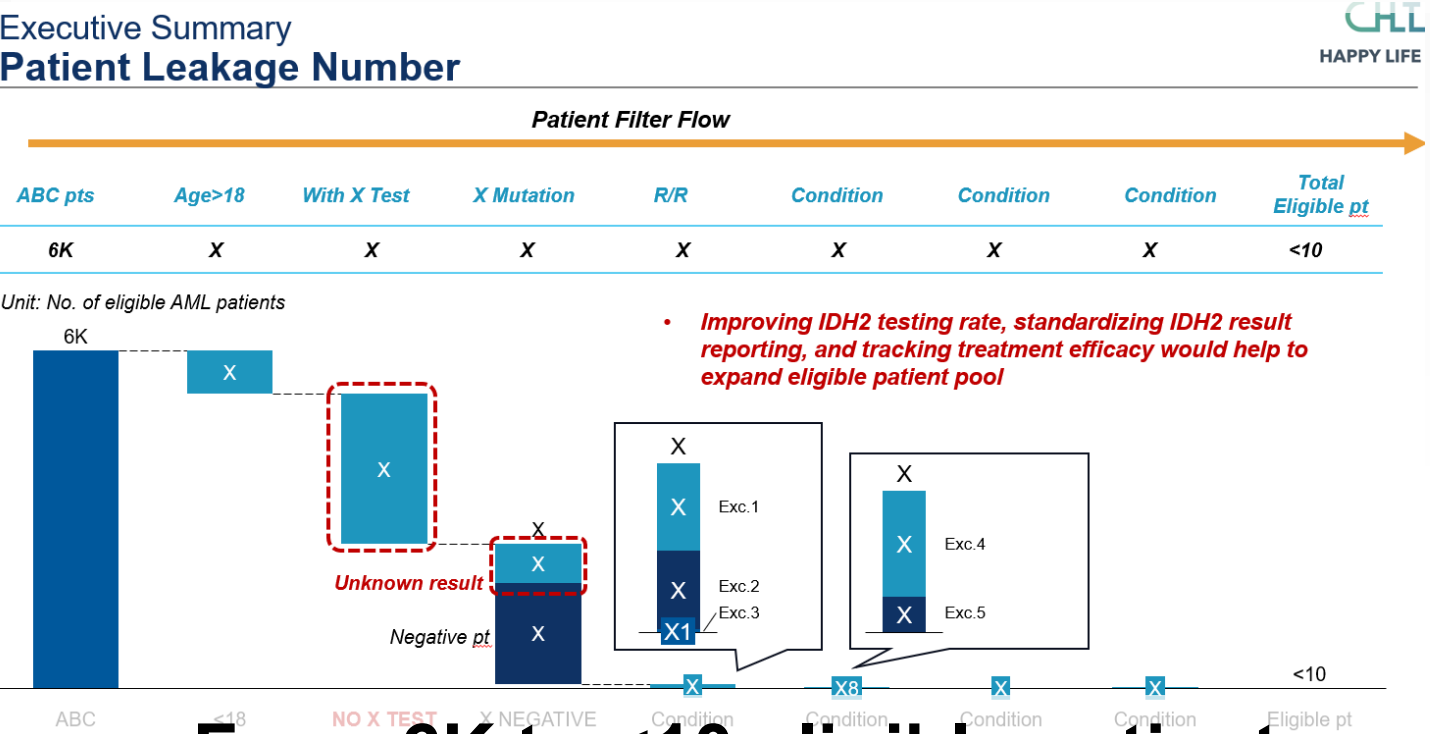
SOURCE: HLT experience; HLT RWD platform

Precise patient identification, deep-dive into undiscovered eligible patient pool and site activation planning drove trial optimization

Precise Recruitment

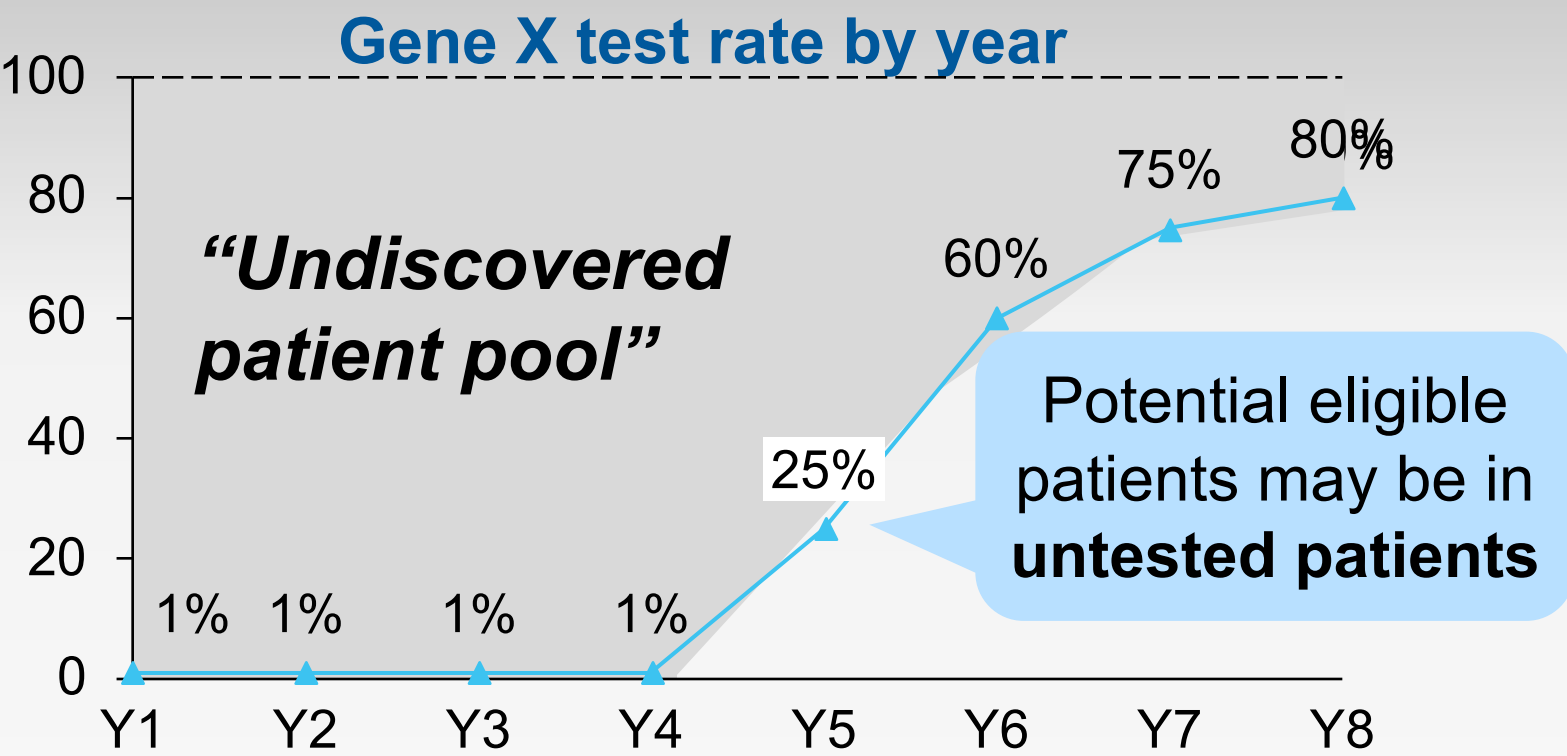


Inclusion / exclusion criteria logic tree, translate protocol into algorithm

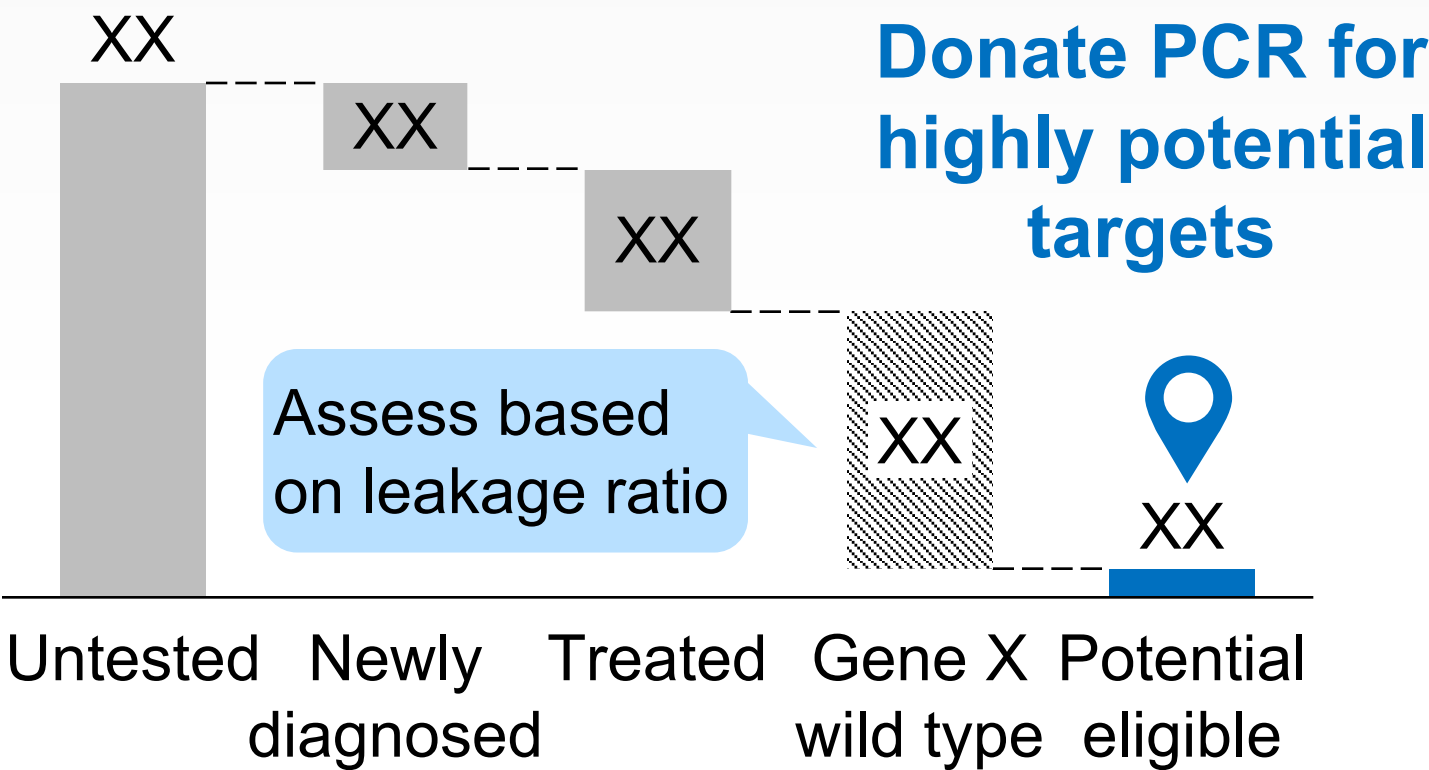


From 6K to <10 eligible patient

“Digest” Undiscovered Pool



Discover targets among untested pool



Site Activation

Patient Potential by Hospital



- 1 Some top sites are missed, based on traditional feasibility solution
- Physician can’t correctly assess recruitment efficiency
- 2 Sponsor mis-selected sites of limited subjects

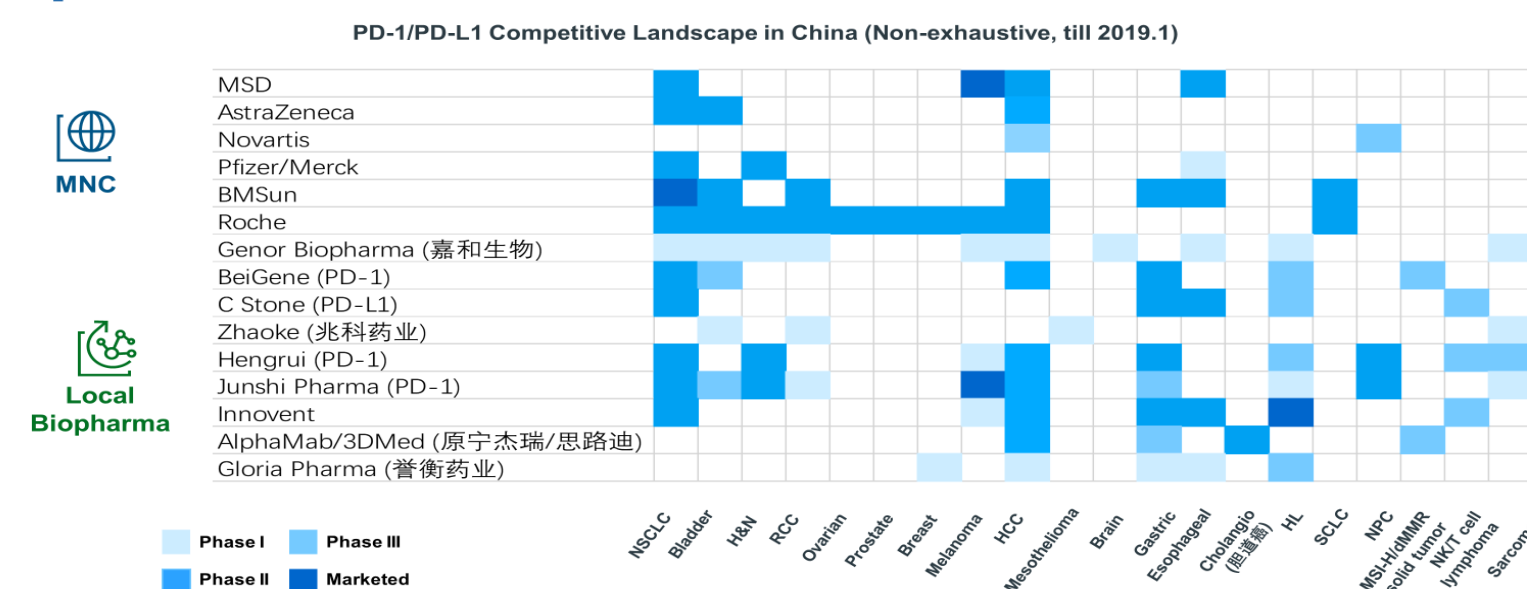
RWD analysis refined site selection

Identifying valuable insights in the highly competitive & dynamic IO market calls for innovative monitoring & analyzing approach

Competitive & Dynamic

- Multiple brands
- Various and subdivided indications

PD-(L)1 therapies in China have already developed to advanced stage and penetrated into broad tumor types



- Complicated combo use
- Widely Off - label use
- Complex usage
- Flexible R&D strategy/RCT/RWE

Unique strategic challenge

- 1 Who are the target patients? How big is the patient size? Where are they?
- 2 Which departments are target patients in? When do they initiate IO therapy? What's the drivers for HCP's prescription? How about administration and dosage?
- 3 How does the competitors performance in this market? What's our competitive strategy?
- 4 Which indication can be approved in next 5 years?
- 5 How to seize the first-mover advantage of innovative medical insurance payment among competitors ?

Continuously analyzing IO market is an “explorative pilot” to fully understand the value of accumulative RWD of IO for the pharm



Our purpose

By constantly tracking the patients cohort using different IO products , we are expected to establish a database with accumulating RWD

Keep diving deep into the database to explore all kinds of insights (RD, MKT, Sales, Access, M.A.)



How to build/manage cohort

Include all IO users' data

Build up subgroups:

- Local patients
 - Regular in-patients
 - Out- & In-patient
 - Only out patients
- Migrant patients
 - Repeatedly visit
 - Single visit

Continuously tracking and analyzing algorithm



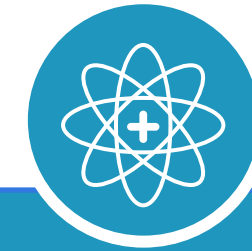
How to mine data

From fragmented data (HIS/LIS) into structure RWD

From RWD into IO research purpose database (~370 fields)

Build up open query-base service model

Apply advanced analytic method



Values to pharm

Find insightful findings, and initiate in-depth exploration

Conduct real world study to generate high quality evidence

Make HTA to support NRDL listing

Optimize evidence generation strategy including RCT + RWE + PCRO

Example: how real world patient EMR database could provide values

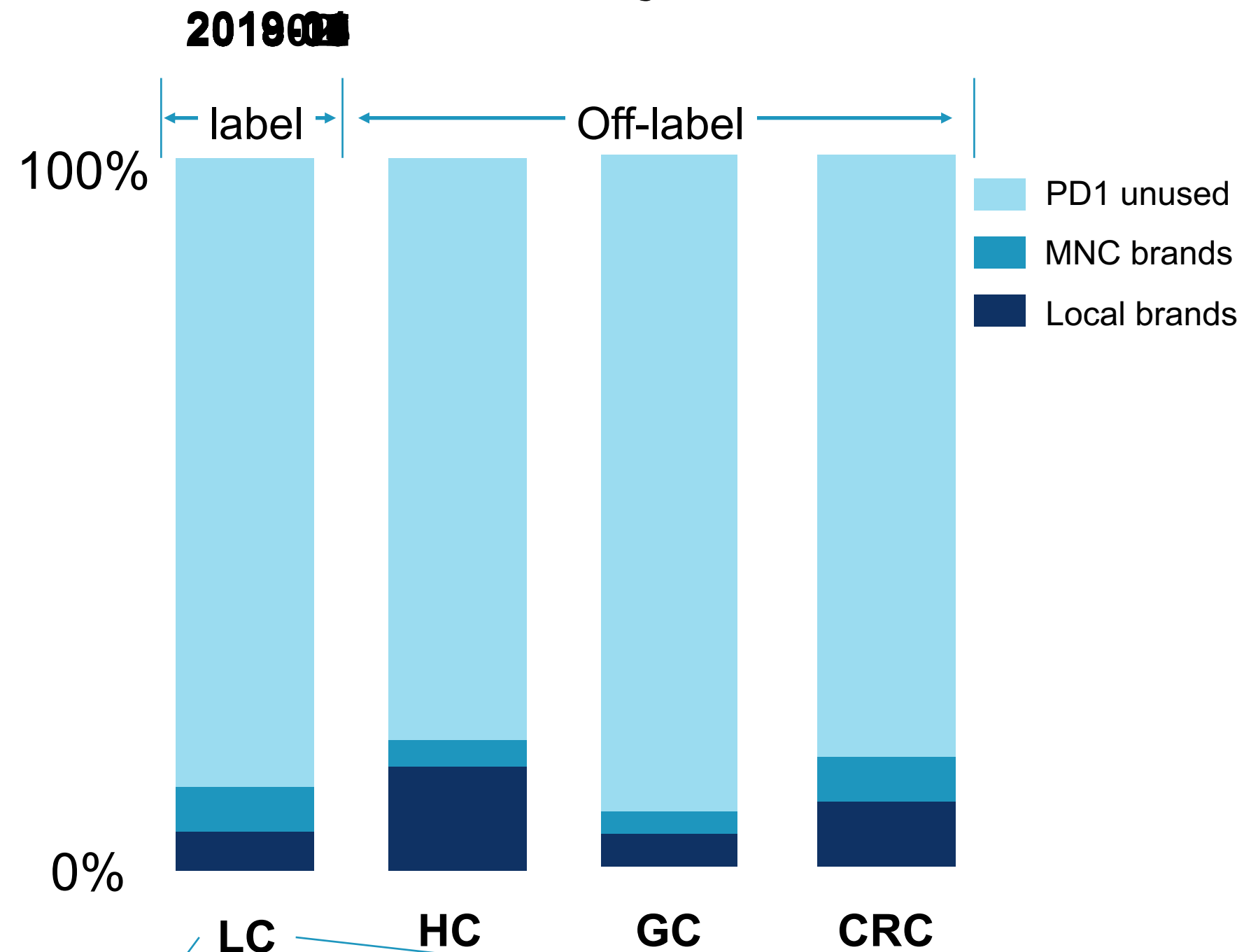
For example, the treatment process for a lung cancer patient ended up with I/O therapy



RWD can further track the patient penetration and competitor landscape to understand market evolution pattern

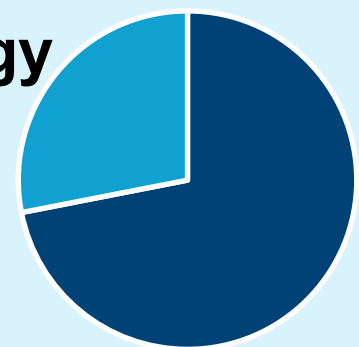
PD-1 penetration by Cancer Type

Evolution by Time

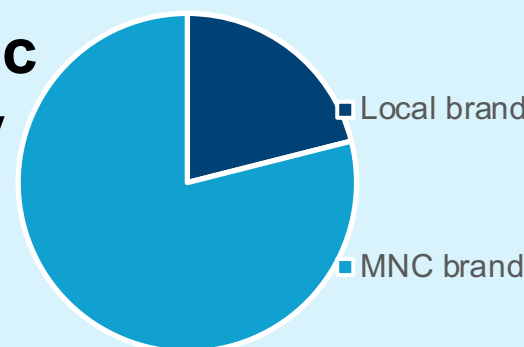


Further Deep-Dive on Competitor PD-1 Usage Distribution by Departments by Cancer Types

Oncology dept.

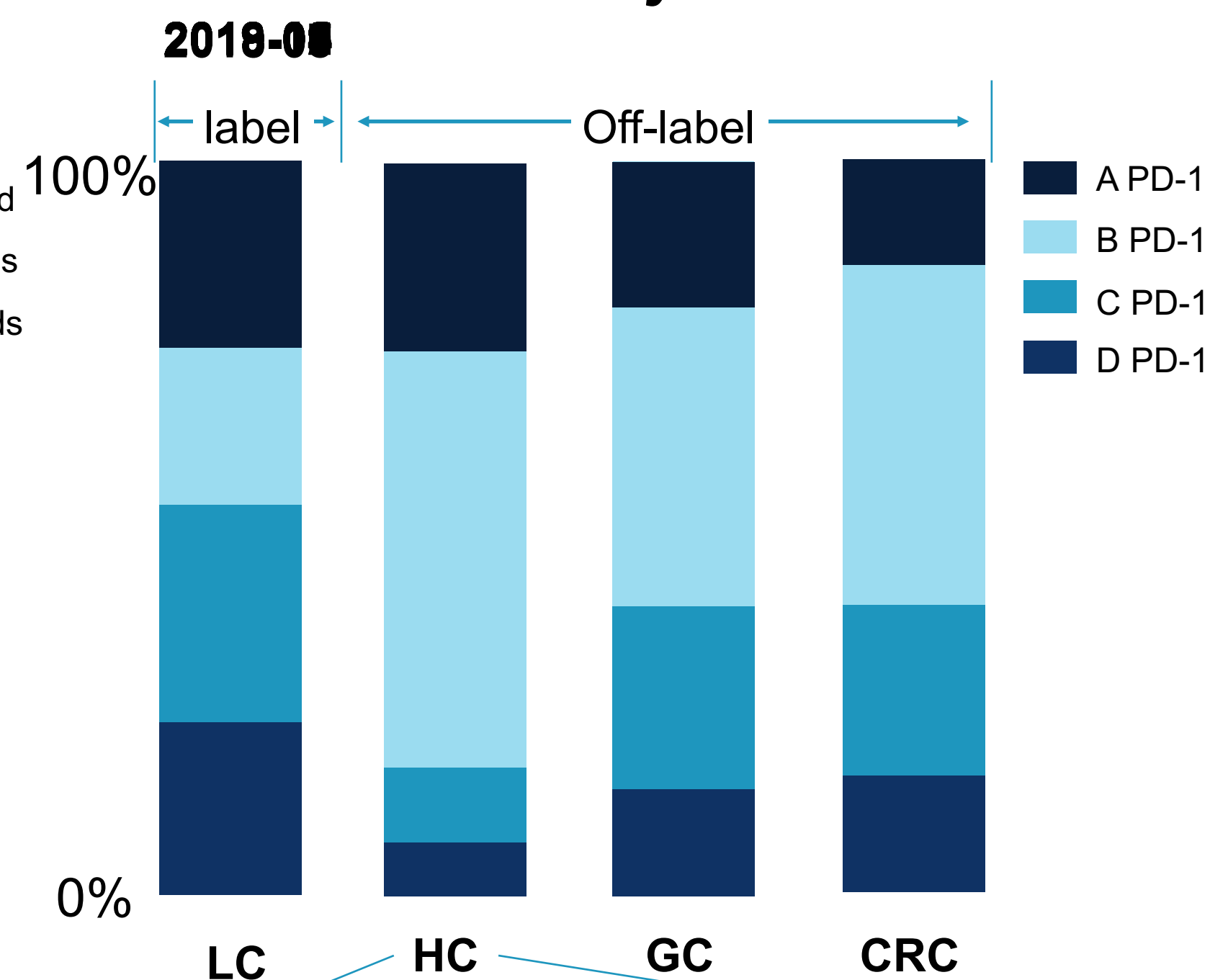


Thoracic surgery dept.



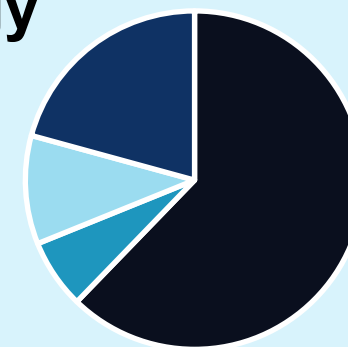
Brand share of PD-1 products

Evolution by Time

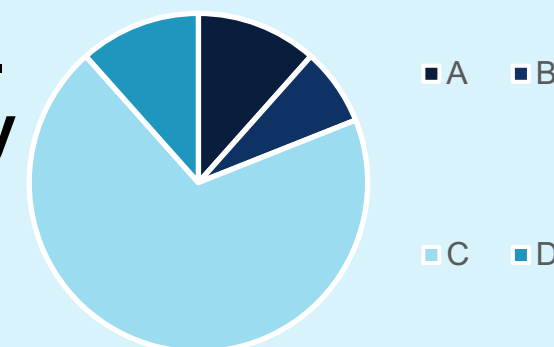


Further Deep-Dive on Competitor PD-1 Usage Distribution by Departments by Cancer Types

Oncology dept.



Gastro. surgery dept.

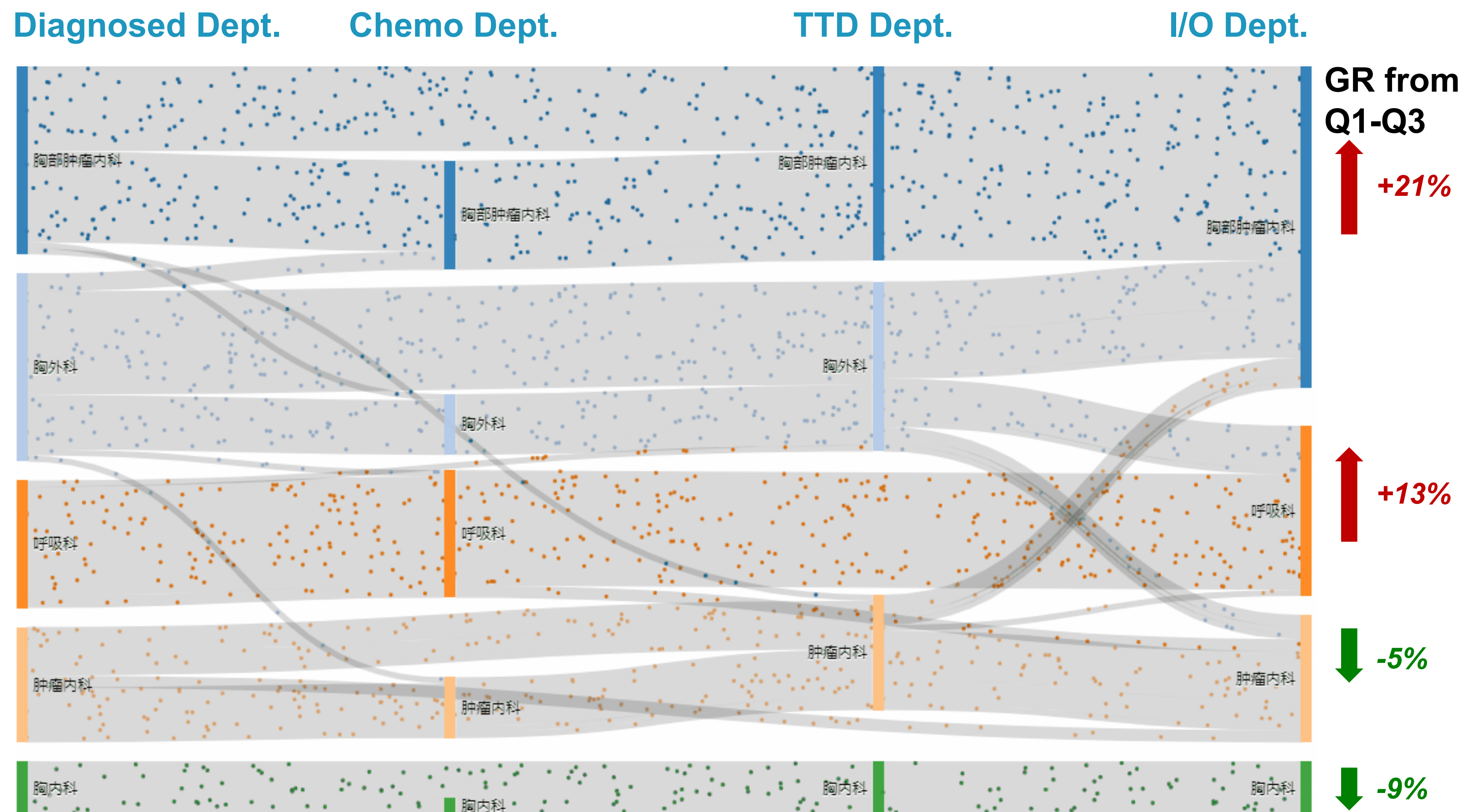


Value

- **Continuously track** the trend of “department X indication” in key market
- **Dynamically monitor** the off-label use or new opportunity department to generate insights
- **Precisely understand** the market size and potential in a hierarchical framework
- Multiple **competitors** can be included in the analysis

How patient flow analysis could help the pharm

Department Referral

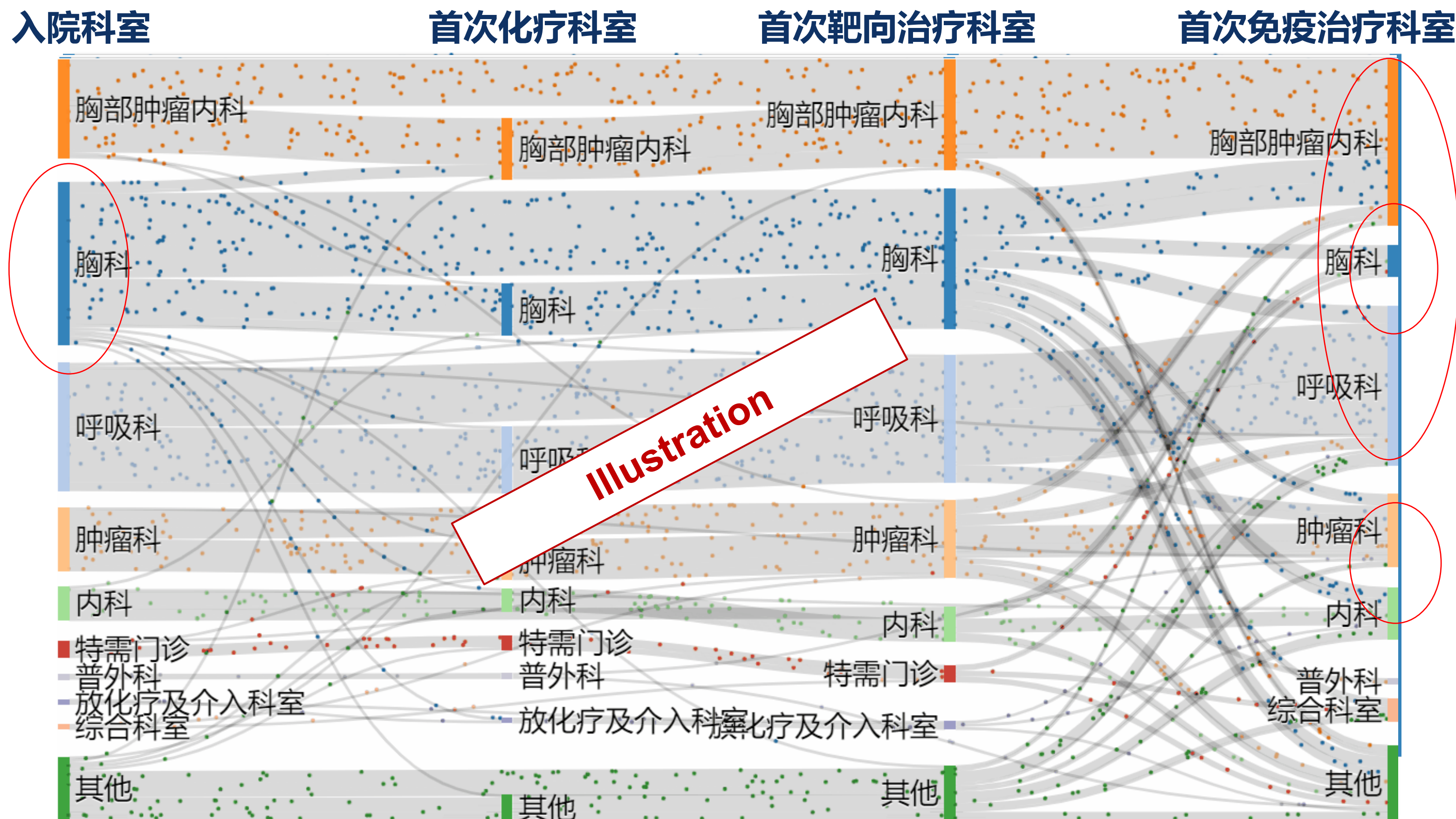


Value

- Precisely identify patient “initiation departments/IO启动科室”, key “referral departments/患者转诊科室”, key “synergy department/IO治疗协同科室”, “current high-potential department/已知高潜力科室”, “high-potential department in the future/未来高潜力科室”
- Combined with the competitive analysis to reveal more insightful findings in a war game map

Case: Identify departments with high concentration of adopting I/O and departments with higher I/O referral rate

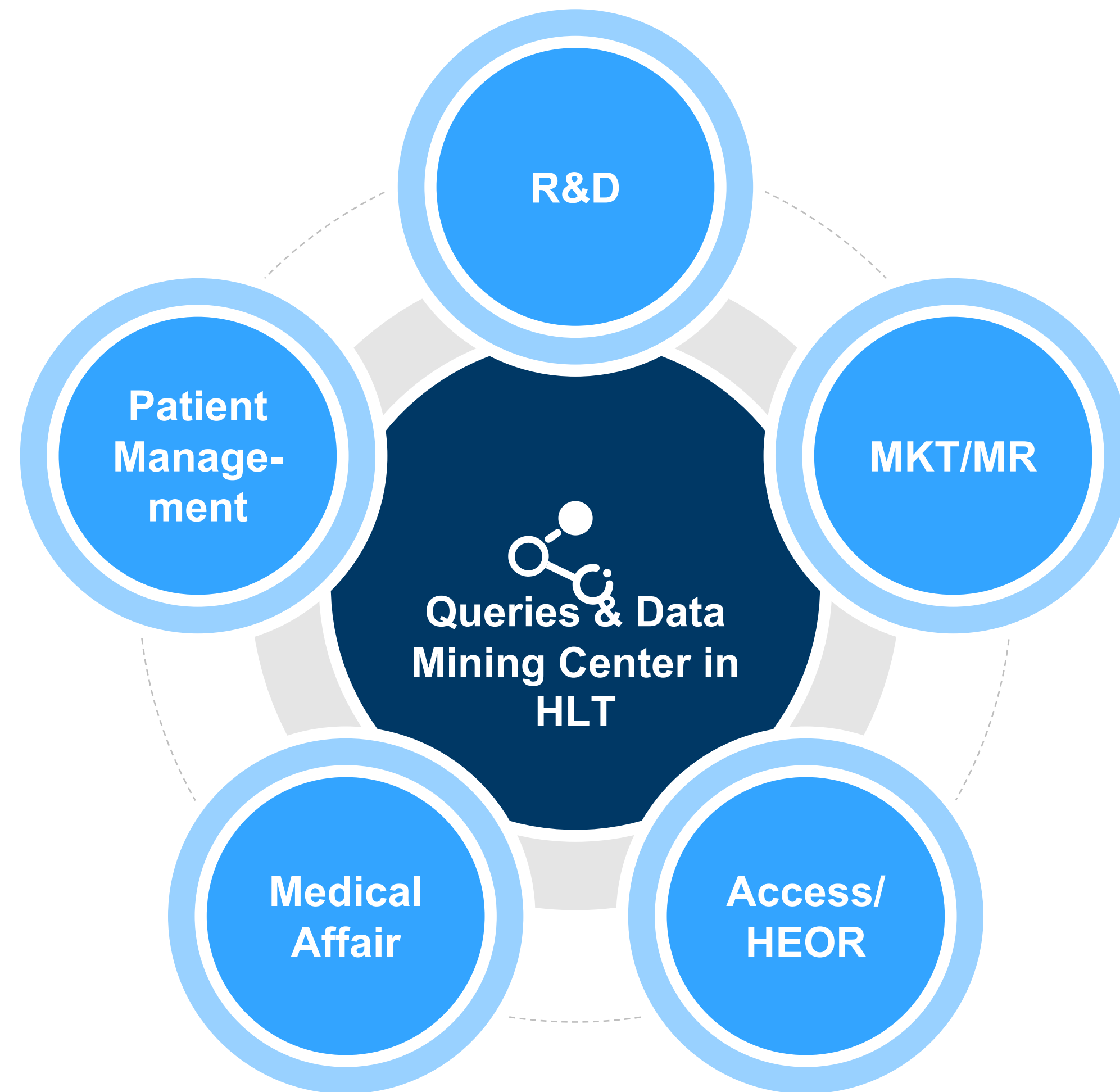
I/O Patient Departmental Treatment 接受免疫治疗的肺癌患者科室流转图



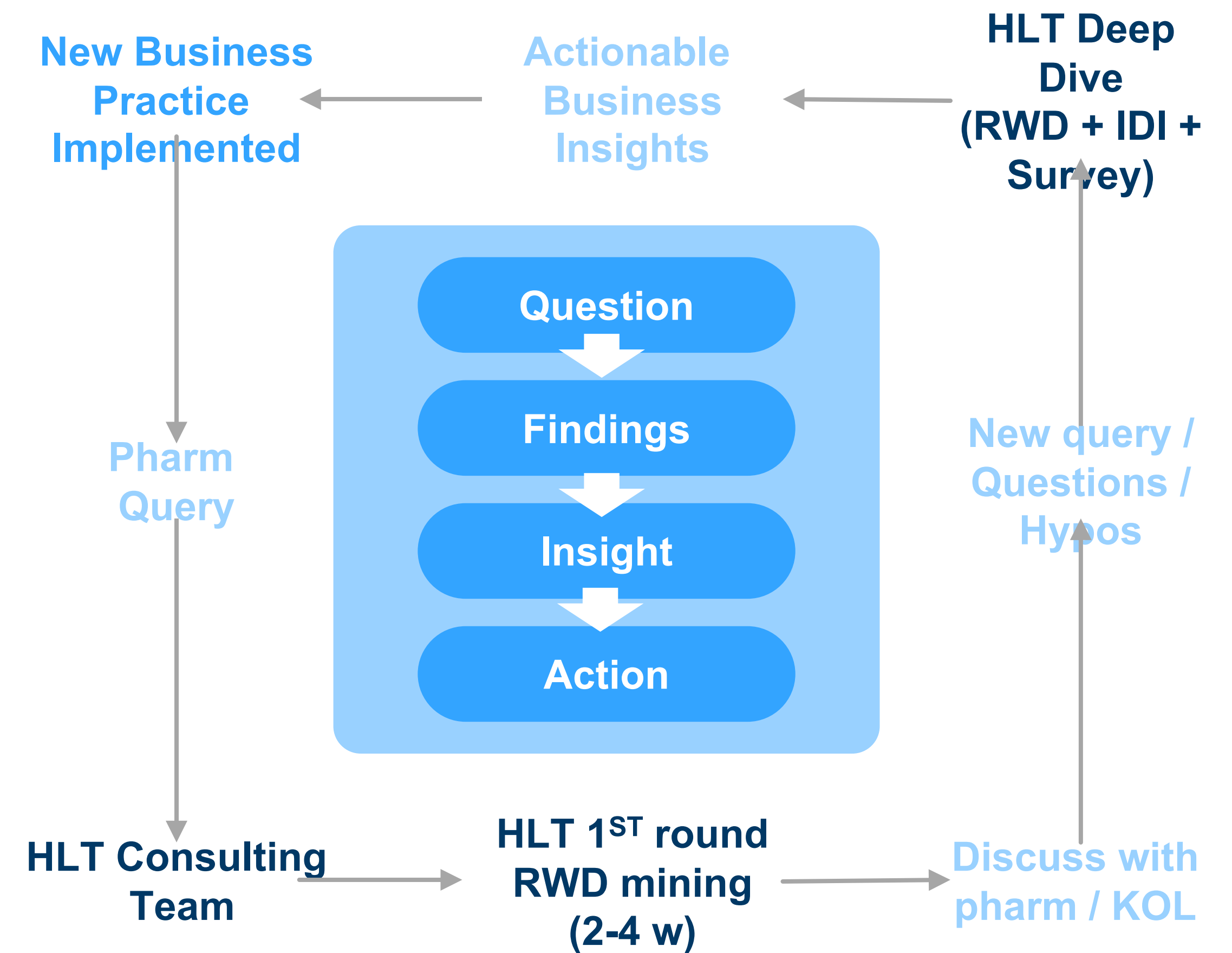
Implications

- I/O lung cancer patients are concentrated in the oncology and respiratory departments
- Thoracic department has significant load of chemo and TKI patient, while less I/O usage. Patients switch to other department for I/O treatment
- Compared with PMR, the RWD approach shows its unique value with departmental scalability and unified standard

How to fully leverage this? A new collaboration model: query-base-participative collaboration model



Query-base, Participative Collaboration Model



More directions our R&D team is exploring (relevant to pharma with oncology asset business, non-exhaustive)

- 1 Customized market segmentation analysis based on **different treatment mindsets (switch of line)** in a unestablished market (MM for example)
- 2 Real world insight mining to support mature chemo to **extend label** into new administration, new patient sub group, new treatment line or new combo therapy
- 3 Comparing non-guideline-recommended regimes' **real world effectiveness & safety** vs. guideline recommended SoC to generate insights for **market shaping** (drive molecule share, DoT, penetration in lower tier hospitals)
- 4 **Patient leakage, dosage & compliance tracking** for IO products to comprehensively understand business potentials and right approaches to drive growth (drive new patient #, drive dosage, drive cycle #, optimize PAP design, develop innovative payment scheme)
- 5 Help hospital presidents or head of pharmaceutical department develop **management tool of data tracking & reporting** to meet MoH's report requirement to drive **KA breakthrough**



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